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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,416	05/19/2005	Jaume Pinol Ribas	Q-87778	7473

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EXAMINER	
SHAHNAN SHAH, KHATOL S	

ART UNIT	PAPER NUMBER
1645	

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02/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,416	RIBAS ET AL.	
	Examiner	Art Unit	
	Khatol S. Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-29* is/are pending in the application.

4a) Of the above claim(s) *18 and 20-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-17 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/19/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 13-29 are pending in this application. Claims 1-12 have been canceled in a previous amendment.

Election/Restrictions

2. Applicants' election with traverse of 11/01/2007 is acknowledged. Applicants elected group I (claims 13-19) drawn to an immunogenic *Actinobacillus pleoropneumoniae* APP strain and a vaccine composition.

The traversal is on the ground(s) that applicants' recite that "The Examiner contends that restriction is proper because the inventions do not relate to a single general inventive concept that has a common technical feature patentable over the prior art, i.e., the Examiner contends that Reimer et al teaches genes of apxIA and apxIIA of *Actinobacillus pleoropneumoniae.* Applicants hereby elect the invention of Group I, with traverse. In regard to election of species applicants elected (apxIA) claim 16. Claim 18 is withdrawn from further prosecution as being drawn to non-elected species. The Examiner is requested to note that the common technical feature patentable over the prior art is not the noted genes, but a mutation in the noted genes, especially a mutation in the transmembrane domain of ApxI, and optionally also, in the transmembrane domain of ApxII, such that the strain is immunogenic and non-haemolytic. Thus, the claims are directed to mutated genes, not the wild-type genes."

This is not found persuasive. Reimer et al teaches also teach mutations in the apxIA and apxIIA and the apxI CABD operon and non-haemolytic strains (see abstract and page 198). Additionally each group of I-IV as mentioned in the restriction mailed 10/02/2007 has a special technical feature that is not required for the other groups. T

The special technical feature of group I is a strain of *Actinobacillus pleoropneumoniae* APP.

The special technical feature of group II is a strain of *Actinobacillus pleoropneumoniae* CECT 5985.

The special technical feature of group III is a strain of *Actinobacillus pleoropneumoniae* CECT 5994.

The special technical feature of group IV is a method of obtaining an organism.

The requirement is still deemed proper and is therefore made FINAL. Claims 13-17 and 19 are under consideration. Claims 18 and 20-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions.

Specification

3. The disclosure is objected to because of the following informalities:

The use of the trademarks Stratagene etc have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants' cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Appropriate corrections are required.

Information Disclosure Statement

4. The information disclosure statement filed 5/19/2005 has been considered. An initialed copy is enclosed.

Priority

5. Acknowledgment is made of applicants' claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. Spain

P200202663, filed on 11/20/2002. However, no translation of said application has been filed. For the purpose of prior art the priority date will be granted as the filing date of PCT application of 11/17/2003.

Drawings

6. The drawings and replacement sheets filed 5/19/2005 have been approved by the examiner.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 13-17 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Non-hemolytic *Actinobacillus pleoropneumoniae* strains comprising a mutation in a least in one region of a gene can be found in nature.

The claimed invention is drawn to a product of nature. Products of nature are not patentable because they do not reflect the "hand of man" in the production of the product or manufacturing process. Diamond v. Chakrabarty. 206 USPQ 193 (1980). Additionally, purity of naturally occurring product does not necessarily import patentability. Exparte Siddiqui 156 USPQ 426 (1966). However when purity results in new utility, patentability is considered. Merck Co. V. Chase Chemical Co. 273 F. supp 68 (1967). See also American Wood v. Fiber Disintegrating Co, 90 U5 566 (1974): American Fruit Growers v. Brogdex Co 283 U5 1 (1931). Funk brothers seed Co. V. Kalo Innoculant Co. 33 U5 127 (1948). Filing of arguments and evidence of a new utility imparted by the increased purity of the claimed invention and amendment to the claims to recite the essential purity of the claimed products is suggested to obviate the rejection. For example. "An isolated product..."

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim19 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunogenic , non –haemolytic *Actinocacillus pleoropneumoniae* strain comprising a mutation in at least in one region of apxIA and **optionally** a mutation in at least one region of apxIIA genes, does not reasonably provide enablement for a vaccine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP) 2164.01(a). Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples (6) the quantity of experimentation, (7) the relative skill of those in the art, and (8) the breadth of the claims.

Claim19 is drawn to a vaccine. Dorland's Medical Dictionary (29th Edition, 2000) defines "vaccine" as "a suspension of attenuated or killed microorganisms (bacteria, viruses, or rickettsiae), or of antigenic proteins derived from them, administered for the **prevention, amelioration, or treatment of infectious diseases**. In the instant case the applicants' invention is not enabled for the **prevention, amelioration, or treatment of all infectious diseases**. And one skilled in the art will not be able to make/and or use the invention without undue experimentation commensurate in scope with the

claims. The specification fails to teach how to formulate and use the claimed vaccines. The term "vaccine" encompasses the ability of the specific antigen to induce protective immunity to infection or disease induction. The specification does not provide substantive evidence that the claimed vaccines are capable of inducing protective immunity. This demonstration is required for the skilled artisan to be able to use the claimed vaccines for their intended purpose of preventing infections. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed vaccines, i.e. would not be able to accurately predict if protective immunity has been induced. The ability to reasonably predict the capacity of a single bacterial immunogen to induce protective immunity from in vitro antibody reactivity studies is problematic. Ellis, R.W. (Chapter 29 of "VACCINES" [Plotkin, S.A. et al. (eds) published by W.B. Saunders company (Philadelphia) in 1988, exemplifies this problem in the recitation that "the key to the problem (of vaccine development) is the identification of the at protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies"(see page 572, second full paragraph). Unfortunately, the art is replete with instances where even well characterized antigens that induce an in vitro neutralizing antibody response fail to elicit in vivo protective immunity. See Boslego et al. wherein a single gonococcal pillin protein fails to elicit protective immunity even though a high level of serum antibody response is s induced (page 212, bottom of column 2). Accordingly, the art indicates that it would require undue experimentation to formulate and use a successful vaccine without the prior demonstration of vaccine efficacy.

"The skilled artisan in the protein purification art requires much more from a disclosure, at the very characteristic of the protein before even a preliminary purification approach could be devised. By the CAFC's holding in In re Eli Lilly and Co., (Fed. Cir. 1990), a general disclosure must contain a sufficient teaching of how to obtain the claimed results or assurance that a particular results would be obtained if certain directions were pursued. The purification of any protein involves many steps, which often must be practiced in a precise order and under specific conditions of time,

temperature, volume, concentration etc. These steps are not self-evident, and will vary, a great deal from protein to protein. There are literally infinite combinations of possible columns, gradients, gels, precipitants, centrifugations, all with buffers of varying pH, salt concentrations of same, etc., to choose from. Until a purification has been accomplished, and the protein described with some certainty, there is little guidance as to where on would even begin." (IN: Critical Synergy: The Biotechnology Industry and Intellectual Property Protection, Biotechnology Industry Organization, October 17, 1994, page 101).

Applying the above test to the facts of record, it is determined that 1) the nature of invention is an immunogenic complex comprising mutated genes 2) the state of the prior art shows the lack of information using the complex for proper vaccine use 4) The amount direction or guidance presented in the specification is limited to production of apxIA and apxIIA 5) there are no working examples which suggest the desired results producing vaccine composition in **preventing and treating** disease except a very limited experiment in pigs 6) the relative skill of those in the art is commonly recognized as quite high (post – doctoral level).

In conclusion the specification does not support the broad scope of the claims, which encompass recombinant forms and any isolated phages. Thus, applicant has **not** provided sufficient guidance to enable one of ordinary skill in the art to how to make and use the claimed invention in manner reasonably correlated with the scope of the broad claims.

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to make and use the Invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent
in the United States.

12. Claims 13-17 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by MacInnes et al. US 6,019,984

Claims are drawn to an immunogenic, non-hemolytic *Actinobacillus pleoropneumoniae* strain comprising a mutation in a least in one region of the apxIA gene and optionally a mutation in a least in one region of the apxIIA gene.

MacInnes et al. teach immunogenic, non-hemolytic *Actinobacillus pleoropneumoniae* strains comprising a mutation in a least in one region of the apxIA gene and optionally a mutation in a least in one region of the apxIIA gene (see abstract and claims and columns 1-4). MacInnes et al. teach deletion mutations, apxIA and apxIIA (see claims 6-12 and column columns 3 and 4 and figures). As to product of claim 19 and product of MacInnes et al. they are indistinguishable (see columns 13-14). MacInnes et al. teach do not explicitly teach nucleotides 886 to 945 of apxIA gene, however, such limitation would inherent in the full sequence of apxIA taught by MacInnes et al. The prior art anticipates the claimed invention.

13. Claims 13, 14, 15, 17 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Prideaux et al. US 6, 0472,183 B2.

Claims are drawn to an immunogenic, non-hemolytic *Actinobacillus pleoropneumoniae* strain comprising a mutation in a least in one region of the apxIA gene and optionally a mutation in a least in one region of the apxIIA gene.

Prideaux et al. teach immunogenic, non-hemolytic *Actinobacillus pleoropneumoniae* strains comprising a mutation in a least in one region of the apxIA gene and optionally a mutation in a least in one region of the apxIIA gene (see abstract and claims and columns 1-2). Prideaux et al. teach deletion mutations, apxIA and apxIIA (see claims 1-4 and column columns 3 and 4). As to

product of claim 19 and product of Prideaux et al. they are indistinguishable (see columns 8, 20 and examples 5-6). The prior art anticipates the claimed invention.

Status of the Claims

14. No claims are allowed.

Conclusion

15. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (571)-272-0863. The examiner can normally be reached on Monday-Friday 7:30 AM-5:00 PM If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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February 1, 2008

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